REMARKS

Applicant respectfully requests entry of the amendments and remarks submitted herein. Claims 18-21, 30, 32, 40, 52, 56-58 are amended, and claims 1-17, 22-29, 31, 33-39, 42-51, 53-55, 59-79 are canceled. Therefore, claims 18-21, 30, 32, 40-41, 52, 56-58 and 80-82 are currently pending.

Information Disclosure Statement

Applicant filed an Information Disclosure Statement on April 30, 2008. The Examiner sent the Applicant a Non-Final Office Action on July 7, 2008 enclosing copies of Information Disclosure Statements initialed by the Examiner as being acknowledged. However, under Non Patent Literature Documents, the Examiner did not initial the citation for the European Search Report, European Application No. 03 78 6836, dated 3/19/08. Applicants requests the Examiner consider this reference and return a copy of the initialed Information Disclosure Statement.

Rejection under 35 U.S.C. §112

The Examiner has rejected claims 6-7, 9, 44-45 and 47 under 35 U.S.C. §112 as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6-7, 9, 44-45 and 47 have been cancelled, thereby rendering this rejection moot.

Rejections under 35 U.S.C. §102

1. 35 U.S.C. §102(b) -- Uhrich (WO 99/12990)

The Examiner has rejected claims 1-5, 10, 14, 18, 21, 38-39, 40-43, 48-49, 52 and 58 under 35 U.S.C. §102(b) as being anticipated by Uhrich (WO 99/12990, hereinafter referred to as "Uhrich").

Claims 1-5, 10, 14, 38-39, 48-49 have been cancelled. Claims 18, 21, 40-43, 52 and 58 have been amended to depend either directly or indirectly from claim 80, which was not subject to this rejection. Claim 80 recites a medical device having at least one surface, comprising: 1) a first polymer comprising salicylic acid incorporated into the polymer backbone on all or a portion of the surface, wherein the salicylic acid is disassociated from the polymer upon

hydrolysis; and 2) a second active agent selected from paclitaxel and rapamycin that is dispersed within the polymer matrix of the first polymer such that the second active agent is released upon degradation of the first polymer.

Uhrich does not teach or suggest dispersing paclitaxel and rapamycin within the polymer matrix of the first polymer. Therefore claims 18, 21, 40-43, 52 and 58 are not anticipated by Uhrich. Applicant requests that this rejection be withdrawn.

2. 35 U.S.C. §102(a) -- Sirhan et al. (WO 2002/056790)

The Examiner has also rejected claims 1-5, 10, 11, 13-15, 17-27, 29-43, 48-49, 51-53, 55-58, 80 and 82 under 35 U.S.C. §102(a) as being anticipated by Sirhan et al. (WO 2002/056790, hereinafter referred to as "Sirhan et al.").

Claims 1-5, 10, 11, 13-15, 17, 22-27, 29, 31, 33-39, 42-43, 48-49, 51, 53, and 55 have been cancelled.

Claim 80 recites a medical device having at least one surface, comprising: 1) a first polymer comprising salicylic acid incorporated into the polymer backbone on all or a portion of the surface, wherein the salicylic acid is disassociated from the polymer upon hydrolysis; and 2) a second active agent selected from paclitaxel and rapamycin that is dispersed within the polymer matrix of the first polymer such that the second active agent is released upon degradation of the first polymer. Claims 18-21, 30, 32, 40-41, 52, 56-58, and 82 have been amended to depend either directly or indirectly from claim 80.

35 U.S.C. §102(a) provides that an invention is not novel if "the invention was . . . described in a printed publication . . . before the invention thereof by the applicant." In order to demonstrate anticipation, one must show "that the four corners of a single, prior art document describe every element of the claimed invention." *Net Moneyin, Inc. v. Verisign*, 545 F.3d 1359, 1369, 88 USPQ2d 1751 (Fed. Cir. 2008) (citing *Xerox Corp. v. 3Com Corp.*, 458 F.3d 1310, 1322, quoting *Advanced Display Sys., Inc. v. Kent State Univ.*, 212 F.3d 1272, 1282 (Fed. Cir. 2000)). The court in *Verisign* went on to state that "because the hallmark of anticipation is prior invention, the prior art reference – in order to anticipate under 35 U.S.C. §102 – must not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements 'arranged as in the claim.'" *Verisign* at 1370. The court explained

> The meaning of the expression "arranged as in the claim" is readily understood in relation to claims drawn to things such as ingredients mixed in some claimed order. In such instances, a reference that discloses all of the claimed ingredients, but not in the order claimed, would not anticipate, because the reference would be missing any disclosure of the limitations of the claimed invention "arranged as in the claim." But the "arranged as in the claim" requirement is not limited to such a narrow set of "order of limitations" claims. Rather, our precedent informs that the "arranged as in the claim" requirement applies to all claims and refers to the need for an anticipatory reference to show all of the limitations of the claims arranged or combined in the same way as recited in the claims, not merely in a particular order. The test is thus more accurately understood to mean "arranged or combined in the same way as in the claim."

As an example, the court discussed the facts of the *Ecolochem, Inc. v. Southern California Edison Co.*, 227 F.3d 1361 (Fed. Cir. 2000). In *Ecolochem*, the claim at issue recited the use of hydrazine with a mixed resin bed to deoxygenate water. The Federal Circuit reversed the district court's decision that an invention was anticipated by a reference that taught the use of hydrogen with a mixed bed to deoxygenate water, in conjunction with a separate passage discussing deoxygenating water with, among other things, hydrazine. *Ecolochem* at 1369. After determining that the relevant figures and accompanying text described only the use of hydrogen to deoxygenate water, the court concluded that the reference could not anticipate the claimed invention because there was no link between that figure and the general discussion of hydrazine as a deoxygenating agent. *Id.* In other words, the court concluded that "although the reference taught all elements of the claim, it did not contain a discussion suggesting or linking hydrazine with the mixed bed in the figure, and thus did not show the invention arranged as in the claim." *Verisign* at 1370. "The prior art reference must clearly and unequivocally disclose the claimed invention or direct those skilled in the art to the invention without any need for picking, choosing and combining various disclosures not directly related to each other by the teachings of the cited reference." *Verisign* at 1371 (emphasis in original).

The present situation is similar to that described in *Ecolochem*, and Applicant respectfully asserts that the pending claims are not anticipated by Sirhan et al. Sirhan et al. discusses luminal prostheses that allow for controlled release of at least one therapeutic capable agent. Sirhan et al., Abstract. Sirhan et al. suggest that the source of the therapeutic capable agent could be a polymeric material including therapeutic capable agent moieties as a structural subunit of the polymer. Sirhan et al. at page 8, paragraph [30] and page 29, paragraph [113]. Sirhan et al. incorporates by reference WO 99/12990 (Uhrich), which discloses the use of

salicylic acid in a polymer backbone, with salicylic acid being released upon degradation via hydrolysis of the polymer backbone. WO 99/12990 at page 18, Example VIII. Sirhan et al. also mentions that a second compound "may be administered prior to, concurrent with, or subsequent to the implanting of the device (e.g., prosthesis) of the present invention." Sirhan et al. at page 16, paragraph [62]. The second compound may be in the form of a tablet to be taken orally, a transdermal patch to be placed on the patient's skin, subcutaneously, systemically by direct introduction to the blood stream, by way of inhalation, or through any other pathways and bodily orifices, or may be made available to the intracorporeal body by a catheter. Sirhan et al. at page 16, paragraph [63]; pages 40-41, paragraph [159]. The "second compound" may be, among other things, rapamycin. Sirhan et al. at page 17, paragraph [65]; page 41, paragraph [161].

It should further be noted that Sirhan et al. did not actually prepare any devices comprising a polymer with an active agent incorporated into the polymer backbone. In Examples 1, 2, 3, and 8 of Sirhan et al. a drug was loaded onto a stent by spraying or dipping, and then a copolymer or barrier was deposited over the drug. In Example 4, a matrix solution including a matrix polymer and a therapeutic capable agent was coated onto a stent, and the stent was then coated or sprayed with a top coat of a rate-controlling barrier. In Example 7, a matrix solution including a matrix polymer (CAB) and a therapeutic capable agent (mycophenolic acid) were coated onto a stent, and the stent was then coated or sprayed with a top coat of a rate-controlling barrier (parylene).

Applicant submits that Sirhan et al. does not clearly and unequivocally disclose the claimed invention or direct those skilled in the art to the invention without <u>any</u> need for picking, choosing and combining various disclosures not directly related to each other by the teachings of the cited reference, as required by the Federal Circuit in *Verisign*. Sirhan et al. teaches the coating of a therapeutic capable agent onto a stent and teaches that a second compound can be administered. Sirhan et al., however, do not teach or suggest that rapamycin could be dispersed within the polymer matrix of a polymer comprising salicylic acid incorporated into the polymer backbone, such that polymer comprising salicylic acid incorporated into the polymer backbone is released upon degradation of the salicylic acid polymer. Sirhan et al. certainly do not "clearly and unequivocally" or "without any need for picking, choosing and combining various disclosures not directly related to each other" teach that rapamycin could be dispersed within the polymer matrix of a polymer comprising salicylic acid incorporated into the polymer backbone,

such that polymer comprising salicylic acid incorporated into the polymer backbone is released upon degradation of the salicylic acid polymer.

Thus, Applicant respectfully asserts that the pending claims are not anticipated by Sirhan et al., and request the withdrawal of the rejection of claims 18-21, 30, 32, 40-41, 52, 56-58, 80 and 82.

Rejections under 35 U.S.C. §103(a)

1. 35 U.S.C. §103(a) -- Uhrich (WO 99/12990) in view of Berg et al. (US 5,464,650)

The Examiner has rejected claims 1, 11, 15, 19-20, 22-27, 29, 34-38, 45, 49, 53 and 56-57 under 35 U.S.C. §103(a) as being unpatentable over Uhrich in view of Berg et al. (US 5,464,650).

Claims 1, 11, 15, 22-27, 29, 34-38, 45, 49, 53 have been cancelled. Claims 19-20 and 56-57 have been amended to depend from claim 80, which was not subject to this rejection. As discussed above, claim 80 recites a medical device having at least one surface, comprising: 1) a first polymer comprising salicylic acid incorporated into the polymer backbone on all or a portion of the surface, wherein the salicylic acid is disassociated from the polymer upon hydrolysis; and 2) a second active agent selected from paclitaxel and rapamycin that is dispersed within the polymer matrix of the first polymer such that the second active agent is released upon degradation of the first polymer.

In order to make a rejection under 35 U.S.C. 103(a) the Examiner first must establish a *prima facie* case of obviousness. Three criteria must be met: 1) there must be some suggestion or motivation, either in the reference or in the knowledge generally available to one of ordinary skill in the art, to modify the reference; 2) there must be a reasonable expectation of success; and 3) the prior art reference must teach all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not be based on applicants disclosure. M.P.E.P. §2142.

Uhrich does not teach or suggest dispersing paclitaxel and rapamycin within the polymer matrix of the first polymer. Berg et al. does not remedy the deficiencies of Uhrich either singly or in combination with Uhrich. Berg et al discusses the coating of stents. Berg et al. does not teach or suggest dispersing paclitaxel and rapamycin within the polymer matrix of the first polymer.

Since neither Uhrich nor Berg et al. teach all the features of the presently claimed invention, claims 19-20 and 56-57 are not obvious over Uhrich in view of Berg et al. Applicant respectfully requests that this rejection be withdrawn.

2. 35 U.S.C. §103(a) -- Sirhan et al. (WO 2002/056790) in view of Ragheb et al. (US 6,730,064)

The Examiner has also rejected claims 1-5, 10-11, 13-15, 17-27, 29-43, 48-49, 51-53, 55-58 and 80-82 under 35 U.S.C. §103(a) as being unpatentable over Sirhan et al. (WO 2002/056790, hereinafter referred to as "Sirhan et al.") in view of Ragheb et al. (US 6,730,064).

Claims 1-5, 10-11, 13-15, 17, 22-27, 29, 31, 33-39, 42-43, 48-49, 51, 53, 55 have been cancelled. Claims 18-21, 30, 32, 40-41, 52, 56-58 and 81-82 have been amended to depend either directly or indirectly from claim 80. As discussed above, claim 80 recites a medical device having at least one surface, comprising: 1) a first polymer comprising salicylic acid incorporated into the polymer backbone on all or a portion of the surface, wherein the salicylic acid is disassociated from the polymer upon hydrolysis; and 2) a second active agent selected from paclitaxel and rapamycin that is dispersed within the polymer matrix of the first polymer such that the second active agent is released upon degradation of the first polymer.

An obviousness determination turns on underlying factual inquires involving: (1) the scope and content of prior art, (2) differences between claims and prior art, (3) the level of ordinary skill in pertinent art, and (4) secondary consideration s such as commercial success and satisfaction of a long-felt need. *Graham v. John Deere Co.,* 383 U.S. 1, 17 (1966). The Supreme Court has explained that the Federal Circuit's "teaching, suggestion or motivation" test provides helpful insight into the obviousness question as long as it is not applied rigidly. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 127, S. Ct. 1727, 1741 (2007). Accordingly, under *KSR*, "it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound." *Takeda Chem. Indus., Ltd., v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007).

Applicant respectfully traverses this rejection and asserts that the pending claims are not obvious over Sirhan et al. in view of Ragheb et al. No combination of Sirhan et al. and Ragheb

et al. either singly or in combination disclose the dispersion of rapamycin or paclitaxel within a polymer matrix that has salicylic acid in the backbone, as recited by the claims.

As discussed above, Sirhan et al. does not teach all of the elements of the present invention. Sirhan et al. do not "clearly and unequivocally" or "without any need for picking, choosing and combining various disclosures not directly related to each other" teach that rapamycin could be dispersed within the polymer matrix of a polymer comprising salicylic acid incorporated into the polymer backbone, such that polymer comprising salicylic acid incorporated into the polymer backbone is released upon degradation of the salicylic acid polymer, as recited by claims 18-21, 30, 32, 40-41, 52, 56-58, 80 and 82.

With respect to claim 81, which recites the use of paclitaxel, Sirhan et al. do not mention paclitaxel at all. Ragheb et al. do not remedy the deficiencies of Sirhan et al. Ragheb et al. teach a vascular stent or other implantable medical device that provides a controlled release of a bioactive material into the vascular or other system, or other location in the body, in which a stent or other device is positioned. Ragheb et al. at col. 3, lines 8-13. Ragheb et al. teach positing a coating layer on one surface of the device, positing the bioactive material over the coating layer so that the coating layer provides for a controlled release of the bioactive material, and then positing a porous layer over the bioactive material, where the porous layer also provides for a controlled release of the bioactive material through the porous layer. Ragheb et al. at col. 3, lines 16-24. Ragheb et al. state that "a vast range of drugs, medicaments and materials may be employed as the bioactive material in the layer" (Ragheb et al. at col. 8, lines 7-10), and indicate that paclitaxel could be coated onto stents (Ragheb et al. at col. 14, lines 36-37).

The MPEP at §2142 states the following regarding determining obviousness under 35 U.S.C. §103:

> [t]he examiner must step backward in time and into the shoes worn by the hypothetical "person of ordinary skill in the art" when the invention was unknown and just before it was made. In view of all factual information, the examiner must then make a determination whether the claimed invention "as a whole" would have been obvious at that time to that person. Knowledge of an Applicant's disclosure must be put aside in reaching this determination, yet kept in mind in order to determine the "differences," conduct the search, and evaluate the "subject matter as a whole" of the invention. The tendency to resort to "hindsight" based upon an Applicant's disclosure is often difficult to avoid due to the very nature of the examination process. However, impermissible hindsight must be avoided and

the legal conclusion must be reached on the basis of the facts gleaned from the prior art.

Applicant asserts that when combined, Sirhan et al. and Ragheb et al. do not teach the presently claimed invention. As discussed above, Sirhan et al. teaches the coating of a therapeutic capable agent onto a stent and teaches that a second compound can be administered. Sirhan et al., however, do not teach or suggest that rapamycin or paclitaxel could be dispersed within the polymer matrix of a polymer comprising salicylic acid incorporated into the polymer backbone, such that polymer comprising salicylic acid incorporated into the polymer backbone is released upon degradation of the salicylic acid polymer. Sirhan et al. certainly do not "clearly and unequivocally" or "without any need for picking, choosing and combining various disclosures not directly related to each other" teach that rapamycin or paclitaxel could be dispersed within the polymer matrix of a polymer comprising salicylic acid incorporated into the polymer backbone, such that polymer comprising salicylic acid incorporated into the polymer backbone is released upon degradation of the salicylic acid polymer. As discussed above, Sirhan et al. discusses the possibility of a second compound being administered concurrently with, or subsequently to the implanting of the device and may be in the form of a tablet to be taken orally, a transdermal patch to be placed on the patient's skin, subcutaneously, systemically by direct introduction to the blood stream, by way of inhalation, or through any other pathways and bodily orifices, or may be made available to the intracorporeal body by a catheter. The "second compound" may be, among other things, rapamycin. Thus, one of ordinary skill in the art at the time the application was filed, might have considered substituting paclitaxel (from Ragheb et al.) for rapamycin in the tablet, patch, etc. that was separately administered to the patient (from Sirhan et al.). The references, however, even when combined do not teach or suggest that paclitaxel be incorporated into the matrix of a polymer comprising salicylic acid incorporated into the polymer backbone, as recited by pending claim 81.

Applicant respectfully asserts that claims 18-21, 30, 32, 40-41, 52, 56-58 and 80-82 are not obvious over Sirhan et al. in view of Ragheb et al., and respectfully requests that this rejection be withdrawn.

CONCLUSION

The Examiner is invited to contact Applicant's Representative at the below-listed telephone number if there are any questions regarding this Response or if prosecution of this application may be assisted thereby. If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 50-3503. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extension fees to Deposit Account 50-3503.

Respectfully submitted,

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